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ECHOCARDIOGRAPHY IN PULMONARY EMBOLISM

GRADUATION THESIS

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List of Abbreviations

PE - Pulmonary embolism

ECG - Electrocardiography

VTE - Venous thromboembolism

RV - Right ventricle

LV - Left ventricle

DVT - Deep venous thrombosis

RVEF - Right ventricle ejection fraction

RVFAC - Right ventricle fractional area contraction

TAPSE - Tricuspid annular plane systolic excursion

Sm - Systolic tricuspid annular velocity

Em - Tricuspid early diastolic annular velocity

Am - Tricuspid late diastolic annular velocity

APE - Acute pulmonary embolism

TTE - Transthoracic echo

ICU - Intensive care unit

TEE - Transesophageal echo

PAAT - Pulmonary artery acceleration time

CT - Computed tomography

ESC - European Society of Cardiology

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SUMMARY

Title: Echocardiography in Pulmonary Embolism
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Pulmonary Embolism (PE) is a grave medical emergency that has the potential to be fatal. It is caused by the complete or partial obstruction of the pulmonary arteries and or its branches and may lead to acute life-threatening but potentially reversible right ventricular failure.

The most common cause of pulmonary embolism is Venous Thromboembolism. PE interferes with both the circulation and gas exchange. Right ventricular failure due to pressure overload is considered the primary cause of death.

Pulmonary embolism is a very difficult diagnosis to make because the signs and symptoms are often nonspecific. PE is not a disease on its own per say, rather it is a complication of other systemic hypercoagulability states. In addition to standard diagnostic tools such as D-dimers, compression ultrasonography and CT, today echocardiography is also used in diagnosing PE.

Right ventricular assessments are challenging due to the complex 3-dimensional geometric structure of the ventricle. The dysfunction of the right ventricle directly affects the prognosis in patients with PE so being able to quantify this dysfunction and detect it helps in the choice of treatment. Echocardiography is excellent for assessing right ventricle dysfunction, and as such can help greatly in deciding which treatment to give to which patient and quantify the severity of illness.

Moreover, the ESC has officially recommended the use of echocardiography in high risk patients for the diagnosis of pulmonary embolism and in the choice of thrombolysis.

Keywords: Pulmonary Embolism, Echocardiography, Heart Ultrasound, Diagnosis, Venous Thromboembolism, Hypercoagulability.

1. INTRODUCTION

1.1 GENERAL INTRODUCTION

Pulmonary Embolism (PE) is a grave medical emergency that has the potential to be fatal. It is caused by the complete or partial obstruction of the pulmonary arteries and or its branches [1]. It is a common cardiovascular emergency, which by occluding the pulmonary arterial bed may lead to acute life-threatening but potentially reversible right ventricular failure [2].

1.2 EPIDEMIOLOGY

The epidemiology of PE is difficult to determine because many patients remain asymptomatic, or the diagnosis occurs as an incidental finding, while in some cases sudden death is the first presentation of PE and the diagnosis is not discovered until the autopsy [3].

ECG findings are usually nonspecific, in fact, 33% of patients with PE have a normal ECG. The most common abnormal findings are sinus tachycardia and nonspecific ST-segment and T-wave changes. Changes that strongly suggest PE are strain on the right side of the heart manifesting as T-wave inversion in precordial leads V1 through V4, transient right bundle branch block, sudden onset of atrial fibrillation and right atrial enlargement. The S1Q3T3 pattern (i.e. prominence of the S wave in lead I, the Q wave in lead III, and the T-wave inversion in lead III) suggestive of PE is rarely seen [4]. This is why we revert to other diagnostic methods for a definitive diagnosis of PE.

1.3 PREDISPOSING FACTORS

Predisposing factors can be divided into strong, moderate and weak factors. Strong predisposing factors have an odds ration >10 and include: fractures of the hip, knee replacement, major general surgery, major trauma and spinal cord injury. While moderate predisposing factors with an odds ratio between 2 and 9 are arthroscopic knee surgery, chemotherapy, chronic heart or respiratory failure, hormone replacement therapy, malignancy, contraceptive therapy, previous VTE and thrombophilia. Finally, weak predisposing factors with an odds ration <2 are bed rest lasting more than 3 days, immobility due to sitting as occurs in prolonged car or air travel, increasing age, obesity and varicose veins [2].

A table dividing the predisposing factors for venous thromboembolism according to the ESC follows on the next page. Besides dividing the predisposing factors according to the classification of strong, moderate and weak it also concentrates on whether the factor was avoidable by further diving it based on patient-related and setting-related factors.

Table 1. Predisposing factors for thromboembolism

Accepted and modified from European Society of Cardiology, www.escardio.org/guidelines*

Predisposing factors for venous thromboembolism		
Predisposing factor	**Patient-related**	**Setting-related**
Strong predisposing factors (odds ration >10)		
Fracture (hip or leg)		✓
Hip or knee replacement		✓
Major general surgery		✓
Major trauma		✓
Spinal cord injury		✓
Moderate predisposing factors (odds ratio 2 – 9)		
Arthroscopic knee surgery		✓
Central venous lines		✓
Chemotherapy		✓
Chronic heart or respiratory failure	✓	
Hormone replacement therapy	✓	
Malignancy	✓	
Oral contraceptive therapy	✓	
Paralytic stroke	✓	
Pregnancy/post-partum		✓
Previous VTE	✓	
Thrombophilia	✓	
Weak predisposing factors (odds ratio <2)		
Bed rest > 3 days		✓
Immobility due to sitting (eg. Prolonged car or air travel)		✓
Increasing age	✓	
Laparoscopic surgery (eg. Cholecystectomy)		✓
Obesity	✓	
Pregnancy/antepartum	✓	
Varicose veins	✓	

* Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2014; 35: 3033-3080.

1.4. CLASSIFICATION OF TYPES OF EMBOLISM

Pulmonary Embolism may be a result of a number of different conditions. The most common cause is Venous Thromboembolism (VTE). It is the third most frequent cardiovascular disease with an overall incidence of 100-200 per 100 000 inhabitants per year. Non-thrombotic pulmonary emboli are rare and consist of septic emboli, foreign material emboli, fat emboli after a bone fracture, air emboli, amniotic fluid emboli during pregnancy and malignant emboli.

Septic embolism to the pulmonary circulation is a relatively rare clinical event and is commonly associated with right-sided endocarditis caused by staphylococcus aureus.

Foreign-material embolism includes silicone, broken catheters, guide wires and endovascular stent components. It is increasing in incidence with the increasing use of interventional techniques in modern medicine.

Fat embolism occurs in almost all patients with pelvic or long-bone fractures and in those undergoing endomedullary nailing or placement of knee and hip prostheses, but can also occur during bone marrow harvest, in sickle cell disease, fatty liver disease, pancreatitis and after liposuction. The classical triad of fat embolization is characterized by altered mental status, respiratory distress, and petechial rash occurring typically 12-36 hours after injury.

Air embolism can occur in both the venous and arterial systems. Venous is often the result of an iatrogenic complication of the manipulation of central venous and hemodialysis catheters. The major effect of venous air embolism is the obstruction of the right ventricular outflow tract, or of the pulmonary arterioles, by a mixture of air bubbles and fibrin.

Amniotic fluid embolism is a rare but catastrophic complication unique to pregnancy. The most likely mechanism is that amniotic fluid is forced into the uterine veins during normal labour or when the placenta is disrupted by surgery or trauma. Pulmonary vessels are obstructed by cell groups and meconium and an inflammatory reaction occurs due to the release of active metabolites. Majority of patients develop seizures. Mortality is high – up to 21% even in recent cohort studies.

Tumor embolism is seen in up to 26% of autopsies of patients with solid malignancies, although the diagnosis is rarely made before death.

1.5 PATHOPHYSIOLOGY OF PULMONARY EMBOLISM

Acute PE interferes with both the circulation and gas exchange. Right ventricular failure due to pressure overload is considered the primary cause of death in severe PE.

Pulmonary artery pressure increases only if more than 30-50% of the total cross-sectional area of the pulmonary arterial bed is occluded. Anatomical obstruction and vasoconstriction lead to an increase in pulmonary vascular resistance and a proportional decrease in arterial compliance. The abrupt increase in pulmonary vascular resistance results in RV dilation, which alters the contractile properties of the RV myocardium via the Frank-Starling mechanism. The increase in RV pressure and volume leads to an increase in wall tension and myocyte stretch. RV contraction time is prolonged. Together with systemic vasoconstriction, these compensatory mechanisms increase pulmonary artery pressure, improving flow through the obstructed pulmonary vascular bed and thus temporarily stabilize systemic blood pressure. The prolongation of RV contraction time leads to leftward bowing of the interventricular septum. Small distal emboli may create areas of alveolar hemorrhage resulting in hemoptysis, pleuritic and pleural effusion. This is known as pulmonary infarction. Its effect on gas exchange is normally mild, except in patients with pre-existing cardiorespiratory disease.

2. CLINICAL SIGNS

Symptoms of PE include chest pain, cough, hemoptysis, and dyspnea and syncope [5], while signs include tachypnea (>20/min), tachycardia (>100/min) signs of DVt, fever (>38.5) and cyanosis [2], although at times the clinical presentation tends to be nonspecific. Therefore, diagnostic testing plays a crucial role in the diagnosis. At our disposal we have the chest x-ray, electrocardiogram, D-dimer assay, computed tomography and ventilation-perfusion scan. The gold standard in diagnosing PE is pulmonary angiography [6].

Most clinicians are familiar with the problems of diagnosing PE. There are no PE-specific symptoms or signs exclusively pointing to the right direction. Indeed, the most usual clinical symptoms associated with PE could easily be a sign of another disease entirely. The most common symptoms of PE are summarized in Table 2 on the following page.

Table 2. Clinical characteristics of patients with suspected PE in the emergency department.
Accepted and modified from 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism*

Feature	PE confirmed (*n* = 1880)	PE not confirmed (*n* = 528)
Dyspnoea	50%	51%
Pleuritic chest pain	39%	28%
Cough	23%	23%
Substernal chest pain	15%	17%
Fever	10%	10%
Haemoptysis	8%	4%
Syncope	6%	6%
Unilateral leg pain	6%	5%
Signs of DVT (unilateral extremity swelling)	24%	18%

DVT = deep vein thrombosis.

* Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2014; 35: 3033-3080.

Clinical signs and symptoms can be used to stratify the patients into low, intermediate and high probability groups. The Wells rule and the revised Geneva score are both extensively validated pre-test probability scores. Both scores are composed of easily gatherable variables of predisposing factors, symptoms, and clinical sings resulting in 2 or 3 levels of clinical probability depending on the score chosen.

Table 3 on the following page shows the two most commonly used scoring systems, Wells rule and Geneva score, for determining the clinical pretest probability of pulmonary embolism before proceeding with diagnostic testing.

Table 3. Clinical predicted rules for pulmonary embolism

Accepted and modified from 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism *

Wells rule	**Original version**	**Simplified version**
Previous PE or DVT	**1.5**	**1**
Heart rate ≥ 100 b.p.m.	**1.5**	**1**
Surgery or immobilization within the past four weeks	**1.5**	**1**
Haemoptysis	**1**	**1**
Active cancer	**1**	**1**
Clinical signs of DVT	**3**	**1**
Alternative diagnosis less likely than PE	**3**	**1**
	Clinical probability	
Three-level score		
Low	**0-1**	**N/A**
Intermediate	**3-6**	**N/A**
High	**≥7**	**N/A**
Two-level score		
PE unlikely	**0 – 4**	**0 - 1**
PE likely	**≥ 5**	**≥ 2**
Revised Geneva score		
Previous PE or DVT	**3**	**1**
Heart rate		
75-94 b.p.m.	**3**	**1**
≥ 96 b.p.m.	**5**	**2**
Surgery or fracture within the past month	**2**	**1**
Haemoptysis	**2**	**1**
Active cancer	**2**	**1**
Unilateral lower limb pain	**3**	**1**
Pain on lower limb deep venous palpation and	**4**	**1**
Age > 65 years	**1**	**1**
	Clinical probability	
Three-level score		
Low	**0-3**	**0 – 1**
Intermediate	**4-10**	**2 – 4**
High	**≥11**	**≥ 5**
Two-level score		
PE unlikely	**0-6**	**0 – 2**
PE likely	**≥6**	**≥ 3**

* Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2014; 35: 3033-3080.

3. RIGHT VENTRICLE

3.1. ANATOMY AND FUNCTION

The right ventricle is often divided into three parts: an inlet portion containing the tricuspid valve apparatus, a subpulmonary outlet portion, and a trabeculated apical portion [7]. Because of the low pulmonary artery diastolic pressure, there is very little isovolumic contraction [8]. Despite the fact that the RV wall thickness is only about one third of the LV wall thickness, the cardiac output is approximately the same for the right and left ventricle, with some physiological shunting for the bronchial vessels [9].

The right and left ventricle structures and functions vary significantly mainly due to complex hemodynamic differences in the pulmonary and systemic arterial circulation. Low RV pressure due to the mean pulmonary artery pressure and the pulmonary vascular resistance is one sixth of that of the left ventricle [9]. In accordance with Starling's law, the right ventricle can respond to an acute increase in its workload by dilating. When an increased workload is imposed for a longer period of time the right ventricle hypertrophies[20]. Several factors, such as heart rate, ventricular relaxation and compliance, intravascular volume status, atrial characteristics, LV filling and pericardial constraint, influence RV filling [11]. The normal geometry of the right ventricle produces RV shortening on contraction [12]. The wall of the right ventricle is significantly thinner (normally up to 5mm) than that of the left (up to 10mm), consequently the right ventricle compared to the left has a smaller mass but greater volume.

Because of all mentioned above, the ability of the right ventricle to adapt to an acute increase in pressure in the pulmonary circulation is limited to an average pressure of 40 mm Hg. Any further increase in pressure leads to a linear fall in the stroke volume, that is it causes dysfunction of the right ventricle. In the presence of an intact pericardium, acute RV dilatation interferes with LV contractile performance.

With normal aging, the pulmonary artery pressure and pulmonary vascular resistance increase mildly, secondary to an increase in arterial stiffness of the pulmonary vasculature [13].

3.1. RIGHT VENTRICLE DYSFUNCTION IN PULMONARY EMBOLISM

Acute pressure overload of the right ventricle and its dysfunction is most often seen in patients with pulmonary embolism where the hemodynamic event directly affects the prognosis. The coronary perfusion of the right ventricle in 80% of cases occurs by means of the right coronary artery and its branches during systole and diastole, as opposed to the left ventricle where most of the coronary perfusion occurs during diastole. Acute pressure overload of the RV leads to problems with myocardial perfusion during systole, an increase in oxygen demand of the myocardium and consequent ischemia, myocyte necrosis and additional dysfunction of the systolic function of the RV.

In patients with a previous history of heart or lung disease it is enough for 25-30% of the pulmonary vasculature to be occluded for the pressure in the pulmonary artery to rise significantly. In patients without such a history the obstruction of 50-75% leads to this dysfunction.

Furthermore, hypoxia caused by vasoconstriction also contributes to the pressure increase, as well as the release of vasoactive substances such as thromboxane, histamine, serotonin, etc.

Many clinical researchers have proven beyond the shadow of a doubt that the RV dysfunction in hypotensive and normotensive patients with PE is directly related to early mortality. In Wolde's meta-analysis it was clearly shown that RV dysfunction was related to a two-fold increase in mortality [14].

4. ECHOCARDIOGRAPHY

Echocardiography is most appropriately recommended for patients with hypotension and or shock and suspected pulmonary embolism [5].

Right ventricular assessments are challenging due to the complex 3-dimensional geometric structure of the ventricle, the limited definition of endocardial borders, retrosternal position, and the interrelationship with the left ventricle [15].

Echocardiography offers the advantage of availability and versatility. Assessing RV function based on volumetric approximations of the right ventricle, these models only crudely represent the true RV volume [16].

RV size is often compared to the LV size, which is normally two thirds the size of the left ventricle. Several echocardiographic projections should be used to assess the whole of the right ventricle. McConnell et al reported a segmental RV dysfunction in patients with pulmonary embolism with distinct segmental patterns in RV dysfunction in different diseases such as acute RV myocardial infarction and arrhythmogenic RV dysplasia [17]. A quantitative approach should be attempted for better accuracy, serial assessments, and for comparisons with reference values. The RV ejection fraction (RVEF) is the most frequently used index of RV contractility.

RV fractional area contraction (RVFAC) can be used to determine the RV ejection fraction but it presents a major challenge to accurately trace the RV endocardial borders. Tricuspid annular plane systolic excursion (TAPSE) has been used to study RV dysfunction in different cardiac diseases.

Systolic tricuspid annular velocity (Sm) reflects systolic longitudinal RV function. Tricuspid early (Em) and late (Am) diastolic annular velocities reflect diastolic RV function and can also be used to determine RV filling pressure [18]. One study identified the tricuspid Am, a reflection of the atrial contraction, as being correlated with the pulmonary artery systolic pressure [19], and another showed no difference in tricuspid Am between PE patients and age-matched controls or between PE patients with high and normal systolic pulmonary artery pressures [20].

The isovolumic relaxation time has been shown to be prolonged in patients with pulmonary arterial hypertension compared to patients with lung disease without pulmonary hypertension and healthy subjects [21]

5. ECHOCARDIOGRAPHY OF THE RIGHT VENTRICLE IN PULMONARY EMBOLISM

Echocardiographic findings indicating RV dysfunction have been reported in >25% of patients with PE [2].

Right ventricular enlargement, right ventricular dysfunction, in some cases with preservation of the apical contractility also known as McConnell's sign. If the pulmonary embolism is large, more than 90% of patients have right ventricular hypokinesis [22]. Signs of pulmonary hypertension include flattening of the interventricular septum during systole, tricuspid regurgitant flow velocity higher than 2.7m/sec [5].

In patients with acute PE there is marked prolongation of the isovolumic contraction time and isovolumic relaxation time over the tricuspid annulus [22].

Echocardiographic findings used to risk stratify patients with PE include RV dilation, an increased RV-LV diameter ratio, hypokinesia of the free RV wall, increased velocity of the jet of tricuspid regurgitation, decreased triscuspid annulus plane systolic excursion, or combinations of the above [2]. Meta-analyses have shown that RV dysfunction detected by echocardiography is associated with an elevated risk of short term mortality in patients without hemodynamic instability, but its overall positive predictive value is low. In addition, Echocardiography can also identify right-to-left shunt through a patent foramen ovale and the presence of right heart thrombi, both of which are associated with increased mortality in patients with acute PE.

Due to the presence of embolic material within the pulmonary arteries, a decrease in the preload on the left side of the heart occurs, this can be indicated by a reduced early diastolic mitral flow velocity in patients with confirmed APE as compared to healthy subjects [23].

The choice of diagnostic imaging method in PE depends largely on the 24-hour availability of different methods. Interobserver variability must always be considered in diagnostic methods as it can affect the results.

There are two possibilities for echocardiography in PE: transesophageal echocardiography and transthoracic echocardiography. TTE visualizes intracardiac thrombi and generally does not detect emboli in the pulmonary arteries. Central emboli can be seen by the TEE in about 70% of patients [24]. Because of the limited specificity with the TTE, the invasiveness of the TEE and the low sensitivity with both approaches, echocardiography is not suitable as a routine diagnostic test for PE [25]. In the ICU, however, echocardiography is attractive since it is noninvasive and does not require the transport of an unstable patient [5].

Even if echocardiography is nondiagnostic for PE, it may still provide important information by helping exclude other causes of shock, such as acute left ventricular dysfunction, tamponade, acute valvular disease, and aortic dissection [24,25].

PE-classification includes a high risk group (risk level > 15%), intermediate risk group (risk level 3-15%), and a low risk group (risk level < 1%) [2]. These groups refer

to the early mortality risk which usually entails the first month. Patients belonging to the high-risk group are those that are hemodynamically unstable with shock or hypotension. High risk PE is an immediately life-threatening situation, and patients presenting with shock or hypotension are a distinct clinical problem. Hemodynamic instability encompasses patients with RV overload, shock and resulting low systemic output that requires resuscitation, that is, hemodynamic and respiratory support. These patients require emergency diagnostic evaluation in order to commence treatment, firstly pharmacological (or, alternatively surgical) and reperfusion therapy. Patients without shock or hypotension that are not at high risk of an early adverse outcome fall into the categories of intermediate or low risk. A clinical prognostic score, the PESI (Pulmonary Embolism Severity Index) was devised for such cases. This is summarized in table 4. Using this scoring system patients are further stratified. In people who display evidence of both RV dysfunction and elevated cardiac biomarker levels in the circulation (particularly troponin) should be classified as intermediate-high risk category. On the other hand, patients with normal RV on echocardiography and normal biomarkers belong in the intermediate-low risk group. Patients in the low risk group are those that do not have shock or hypotension and after performing the PESI scoring have a low mortality risk, they may however have observable signs of PE on echocardiography as well as elevated cardiac biomarkers. RV dilation is found in at least 25% of patients with PE, and its detection is useful for risk stratification of the disease [2]. Acute RV dysfunction is a critical determinant of outcome in acute PE and this is where echocardiography comes into play. In high risk patients echocardiography may be diagnostic, but it is not diagnostic in patients with PE that have preserved blood pressure. In those patients we can find RV dysfunction (measured by

echocardiography, as well as troponins or BNP) which may help us with our prognosis and point to a greater need for ICU treatment. This is a very important role of echocardiography, not as a diagnostic, but as a prognostic tool.

Table 4. Pulmonary embolism severity index

Accepted and modified from 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism *

Pulmonary embolism severity index (PESI)

Parameter	Original version	Simplified version
Age	Age in years	1 point (if age > 80 years)
Male sex	+10 points	-
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate > 110 b.p.m.	+20 points	1 point
Systolic blood pressure < 100 mmHg	+30 points	1 point
Respiratory rate > 30 breaths per minute	+20 points	-
Temperature < 36 ° C	+20 points	-
Altered mental status	+60 points	-
Arterial oxyhaemolgobin saturation < 90%	+20 points	1 point
	Risk strata	
	Class I: < 65 points Very low 30-day mortality risk (0-1.6%) Class II: 66-85 points Low mortality risk (1.7-3.5%) Class III: 86-105 points Moderate mortality risk (3.2-7.1%) Class IV: 106-125 points High mortality risk (4.0-11.4%) Class V: >125 points Very high mortality risk (10.0-24.5%)	0 points= 30-day mortality risk 1.0% (95% CI 0.0%-2.1%) >1 point(s)=30-day mortality risk 10.9% (95% CI 8.5%-13.2%)

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Venous thromboembolism is manifested most frequently by deep vein thrombosis or by PE. PE is a common and potentially lethal condition with an age-related increase in incidence [26]. Precise figures for the incidence of PE are not available due to non-specific clinical presentation and an unknown number of clinically silent emboli, leading to the conclusion that the actual disease frequency is underestimated.

Echocardiographic findings based on either a disturbed RV ejection pattern (the so called 60-60 sign) or on depressed contractility of the RV free wall compared with the RV apex (the McConnell sign) were reported to retain a high positive predictive value for PE, even in the presence of pre-existing cardiorespiratory disease. Additional echocardiographic signs of pressure overload may be required to avoid a false diagnosis of acute PE in patients with RV free wall hypokinesia or akinesia due to RV infarction, which may mimic McConnell's sign. [2]

An obstruction of more than 30% of the pulmonary vascular bed leads to morphological and hemodynamic changes that can be detected by echocardiography. Echocardiography is a non-invasive, and harmless method for monitoring patients. The most frequent echocardiographic marker is acute pressure increase in the right heart with large pulmonary artery emboli and dilatation of the right ventricle. This dilatation occurs as a compensatory mechanism of the elastic ventricle in order to maintain the stroke volume. These changes can be seen best in an apical projection of the four chambers where one can easily compare the size of the right ventricle with that of the left. In normal conditions, the right ventricle is about 2/3 the size of the left ventricle.

According to various authors, the dilation of the right ventricle is defined as an end-diastolic diameter greater than 27 mm.

Given that the compensatory mechanism of dilation is limited, an acute increase in the pressure of the right ventricle can also lead to the shift of the interventricular septum from the right to the left side which can be seen during systole and diastole, the left ventricle becomes more “D” shaped. When an acute increase in afterload affects one ventricle, the resulting effects on the diastolic pressure-volume relationship of the contralateral ventricle are dependent on pericardial restraint. The normal pericardium can accommodate about a 20% acute increase in cardiac volume before pericardial constraint leads to an increase the ventricular filling pressure and thus septal shift and peripheral circulatory impedance. Therefore, acute distension of the right ventricle during diastole leads to a shift in the LV pressure-volume curve, reflecting decreased LV compliance, which can be the result of a reversal of the transseptal pressure gradient and a marked leftward shift of the interventricular septum which alters the shape of the left ventricle. The shift in the interventricular septum, especially if it occurs during diastole can compromise the diastolic filling of the left ventricle which can in turn lead to an additional hemodynamic worsening of the patient. Therefore, echocardiographic detection of the septal shift is of great importance in the therapeutic decision of fluid compensation with a goal of preventing additional dilatation of the right ventricle.

Disorders of contractility of the right ventricle are another major morphologic marker of acute pressure overload and can best be seen in an apical projection of all four chambers of the heart. The classical image of hypokinesia of the walls was described

by McConnell, which is seen by regionally decreased contractility of the free wall of the right ventricle, while the apex of the right ventricle is normal or even hyperkinetic. This points to a regional ischemia of the lateral free wall of the right ventricle. The specificity of McConnell's sign in diagnosing pulmonary emboli is 94% while its specificity is a mere 20%, and these changes are mainly seen in major pulmonary artery embolism.

The dilation of the right atrium with widened inferior vena cava and hepatic vein can occur as a result of pressure overload of the right ventricle. During inspiration the physiological collapse of the inferior vena cava does not happen in this instance which indirectly reflects the high right heart filling pressure.

The right ventricle in acute obstruction conditions in previously healthy individuals can generate a mean pressure of 40 mm Hg. Massive pulmonary emboli of the pulmonary artery with greater pressures than this lead to acute decompensation of the right ventricle and a state of shock.

From the speed of tricuspid regurgitation one can indirectly calculate the pressure in the right ventricle according to Bernoulli's principle. The speed of flow of the tricuspid regurgitation in a patient with a pulmonary embolism is measured with continuous Doppler. Increased resistance in the pulmonary artery can be proved with the use of a pulsating Doppler in the short parasternal axis by measuring the so-called acceleration time of the pulmonary artery (Pulmonary artery acceleration time) which is shorter in these patients. According to the research by Kurzyna et al the combination of

PA AT < 60 ms and a tricuspid flow pressure < 60 mm Hg shows 94% specificity and 36% sensitivity. The so-called "60/60" sing can increase the sensitivity without compromising the specificity in echocardiographic diagnosis of acute pulmonary embolism.

Overall, echocardiography as a means of diagnosing pulmonary embolism has been shown to have a sensitivity of 50-60%, and specificity of 80-90%. The only sure sign of pulmonary embolism seen by echocardiography is the direct visualization of the embolus at the bifurcation of the pulmonary arteries and in the initial segments of the right and left branches. Large thrombi can lodge at the bifurcation of the main pulmonary artery or the lobar branches and cause hemodynamic compromise at a level of approximately 30-50% of occlusion of the pulmonary bed. Because of the high sensitivity of echocardiography in high risk patients, the current European Society of Cardiology recommends the use of echocardiography as diagnostic method of choice in all patients when it is not possible to perform CT angiography of the pulmonary artery. In patients with low or moderate risk, echocardiography should not be used for diagnosis, but recent studies do mention the importance of echocardiography in the evaluation of right ventricle dysfunction and her effect on the clinical outcome of the illness.

The metaanalysis of Sanchez et al which included five studies with a total of 475 patients testing the prognostic value of echocardiography in risk groups showed a markedly increased risk of early mortality in hemodynamically stable patients with echocardiographic findings of right ventricle dysfunction. The authors, however, state that the results should be interpreted with caution because of the clinical and

methodological diversity of the studies included in the meta-analysis.[27] Wolde et al come to a similar conclusion in their metaanalysis of 7 studies which looked at the interconnectivity between echocardiographically proven RV dysfunction and early clinical outcome of disease [14]. According to them, the studies show an increased risk of mortality of at least 200% in patients with echocardiographically proven RV dysfunction. In contrast to the diagnostic value of echocardiography in hemodynamically unstable patients, in hemodynamically stable patients echocardiography is not recommended for its diagnostic but its prognostic value. In hemodynamically stable patients echocardiography shows a high sensitivity for the diagnosis of RV dysfunction and can play a major role in recognizing patients that require aggressive treatment in intensive care units. The ESC guidelines recommend echocardiography (with or without clinical biomarkers such as Troponins and BNP) for the evaluation of RV dysfunction for the further division of hemodynamically stable patients with increased risk of mortality.

One problem with echocardiography when investigating its value in the diagnosis and prognosis of PE is the lack of standardization of echocardiographic criteria for RV dysfunction. There is a growing demand for a simple, user-friendly approach to detect the RV dysfunction in order to allow a non-expert reader to accurately interpret the echocardiographic findings.

6. CONCLUSION

In conclusion, the dysfunction of the right ventricle directly affect the prognosis in patients with PE so being able to quantify this dysfunction and detect it helps us in our choice of treatment. Echocardiography is excellent for assessing right ventricle dysfunction, and as such can help us greatly in deciding which treatment to give to which patient and quantify the severity of their illness. Finally, the ESC has officially recommended the use of echocardiography in high risk patients for the diagnosis of pulmonary embolism and the choice of thrombolysis, while in hemodynamically stable patients they recommend the use of echocardiography for its prognostic value rather than its diagnostic one, given that it is able to differentiate between intermediate and low risk patients. Overall, this makes echocardiography an indispensable tool in the algorithm for the diagnosis and management of pulmonary embolism.

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BIOGRAPHY

Zrinka Car was born in Dubrovnik, Croatia but moved to Cyprus at the age of three with her family. There she pursued her education in St. Mary's School both through primary and secondary school. Her wish was always to return to Croatia and this opportunity arose when she was done with her secondary education. She moved to Zagreb and enrolled in the University of Zagreb, School of Medicine, Medical Studies in English program.

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Her hobbies include volleyball, hiking up Sljeme and spending time with her friends and family.

She is fluent in Croatian, English, Greek, French and Italian.